THE BIOCHEMISTRY OF CONCEPTION CONTROL*

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THIS is not the place to discuss the optimal number of people in any country or in the world, nor is it the place to discuss the possible social consequences of the ability to make pregnancy invariably a matter of deliberate intention. It is clear however that, although the world could no doubt support more people than there are in it now, it could not support an indefinite number (cf. *Four Thousand Million Mouths*, 1951). It is also clear that there are many circumstances in which the ability to control pregnancy would be an advantage.

The words in the title were chosen carefully; we are concerned with control which means not only prevention but also promotion if there is difficulty. The words contraception and birth control were avoided because the former, although in principle it has the required meaning, has taken on a more restricted meaning in popular use, and the latter would extend the subject to include the termination of established pregnancy as well. Not only is the biochemistry of pregnancy a formidable subject but if, like conception, it is examined in both a positive and negative sense, it leads to the discussion of abortifacients and that would broaden the field too greatly. It is obviously better to stop a conception rather than cope with an unwanted pregnancy.

The Ideal

Both at the present time and in the past many methods have been used for controlling conception, but they will be referred to only briefly for few of them are biochemical and still fewer desirable. Thus none of the social arrangements designed to restrict sexual contact or diminish sexual interest are germane. People enjoy sex and are entitled to go on doing so. The enjoyment may sometimes reach levels which those with a different response describe as addiction, but that must be accepted even if it is not welcomed. This fact limits the discussion of methods of control. It makes it necessary to leave alone, to the greatest extent possible, the phenomena of which people are aware while copulating and to be chary of altering the hormone balance, for this greatly influences sexual enthusiasm. A fully satisfactory method of contraception should not obtrude itself; methods that involve an insertion just before copulation, as most present methods do, would not therefore be ideal even if they were in other respects satisfactory. Neither, of course, are permanent or nearly permanent methods such as vasectomy or oophorectomy for, admirable as they are in many circumstances, few people easily accept such a radical solution. The ideal is something which when eaten or injected induces a temporary sterility without other effects. No such substance is known and its discovery is likely to call for much sustained biochemical research. This is not at the moment being undertaken and the main purpose of this paper is to see whether a *prima facie* case can be made out for its inception.

The Problem and Method

First the problem may be briefly stated. Sperm are made in the testis, mature there and in the epididymis and are ejaculated into the vagina whence they move by swimming or bulk movement of semen into the uterus. Mature ova are discharged from the ovary into the mouth of the Fallopian tube. The sperm and ovum, or gametes, move into the Fallopian tube from opposite ends and unite in it; the fertilized ovum, or zygote, then continues down the tube into the uterus. It undergoes some stages of development on the way, but most of its

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development takes place after it has become attached to the uterine wall.

A chain of events as elaborate as this would be expected to contain many weak links and the frequency of involuntary sterility bears out the expectation. A better understanding of the chain would improve treatment of these cases, but our primary interest here is to find weak links that could be weakened still further. The search is for a process that is exceptional, or preferably unique, in its biochemical nature. If such a mechanism can be found it should be possible to inhibit it without upsetting any of the other mechanisms on which normal life and health depend. The evidence is largely gained from experiments with animals and this involves the difficulty that animals differ more from one another and from man in their reproductive behaviour than in most other respects. Thus the rabbit, unlike most other species, normally ovulates only after copulation and in several species sperm can survive in the female tract for weeks or even months, whereas in most species they only survive for a few days. Observations made on one species, therefore, give hints rather than evidence about the behaviour of even a closely related species. From our present point of view therefore it is a pity that the main mass of sound evidence relates to such a remote animal as the sea urchin.

Sperm and Semen

Spermatogenesis in most mammals is temperature sensitive, so that it only proceeds satisfactorily in the scrotum where the temperature is intermittently lower than that of the body as a whole. This peculiarity has excited some interest, but the deliberate maintenance of the testes at constant temperature would be inconvenient. Furthermore there is some evidence that exposure to constant temperature interferes with the production of the testicular hormones. The mechanism of this temperature dependence is unknown, but spermatogenesis is probably controlled by the balance of two or more actions with different temperature coefficients. If this is the mechanism it should be possible, and it would be more satisfactory, to interfere with the balance chemically. Spermatogenesis is controlled by other factors such as the level of thyroid function, but an alteration of this would bring about too general effects to be useful.

In the epididymis the sperm "matures." This noncommittal term covers changes in both morphology and metabolism; thus Lardy, Ghosh and Plaut (1949) find that bull sperm entering the epididymis respire more slowly than those that have passed through it but they can be activated by storage in the epididymis and by extracts from sperm. Sperm that have not undergone these changes seem (Young, 1931) to be less able to cause fertilization, so that fuller investigation might well be profitable.

Several accessory glands are involved in making the seminal plasma and its composition is of the greatest biochemical interest. It contains significant amounts of citrate, fructose, inositol, ergothioneine and phosphatase (Mann, 1951, *a* and *b*). All these substances occur elsewhere in the body, but seldom in such high concentrations and never all together. Fructose can be metabolised by the sperm and probably acts as the main fuel for swimming; the function, if any, of the other substances is obscure. Although all these components may not be essential for the effectiveness of sperm, the general, and probably valid, assumption is that they contribute to it. If therefore the mechanisms responsible for the secretion of these unusual accessory substances could be inhibited, it is possible, though by no means certain, that sperm function would be impaired. The seminal plasma is not only a source of metabolites that may be used by the sperm, it is also a system with enzyme activities of its own. Thus at the instant of ejaculation semen is a mobile fluid, but it quickly coagulates to a gel and then several minutes later liquefies again. This process, which has excited interest since the time of Aristotle (*c.* -330), is now being elucidated and is probably advantageous in carrying semen to the os and ensuring its contact with cervical mucus. Semen that did not clot, or, having clotted, did not liquefy, would probably be less effective.

The ejaculated sperm is clearly the most accessible part of the whole fertilization process. Some people (e.g. Baker, 1935) have in fact written as if contraception were synonymous with sperm killing, and this is the aspect of the subject to which almost all attention has been directed hitherto. This is not the place to discuss all the spermicides that have been used or suggested, but it is perhaps worth while discussing a few of the principles that underlie this type of work. We do not yet know enough about the metabolism of sperm to be able to plan contraception rationally. As soon as we think beyond some simple mechanical barrier we are forced to use the purest empiricism. The problem is superficially similar to that in chemotherapy; two systems exist side by side, the host and the " parasite," which in this case is the sperm. The problem is to inhibit the one without affecting the other. It is more difficult than the chemotherapeutic problem because we have to envisage the regular use of an agent during many years; it is easier because the " parasite " has no independent powers of multiplication.

Empiricism versus Biochemical Understanding

Crude empiricism, that is empiricism unilluminated by established knowledge of the mechanism by which an action takes place, can only work in certain directions. Where tests are easy to do there is perhaps no reason to adopt any other method. Thus in searching for antibiotics thousands of strains of microorganisms are " screened " against a set of test organisms in the hope of finding an efficient producer. There is an old laboratory adage " Anything is worth doing if it is easy enough to do " ; the cynic adds " or if you can find someone else to do it." But where tests are not easy to do this empirical approach is extravagant and it becomes imperative to be more analytical. The process goes in stages. If the problem is, or is being approached as, a chemotherapeutic one, the first stage consists simply of trying everything one can lay ones hands on to see what happens. This was the state of pharmacology nearly to the beginning of this century. Ehrlich wrought a revolution when he thought about the chemical structure of the agents he used and, having found a promising line by random methods, changed the molecule slightly in various ways according to a logical chemical plan till, within that group of substances, he reached optimal activity. This was the method adopted by Baker (1935); it is analytical over the chemical half of the problem, but it leaves the biochemical mechanism of action unconsidered.

The second revolution springs from academic work on enzyme inhibitors and was enunciated as a principle by Woods and Fildes. Drugs act, in part at least, by specific enzyme inhibitions and their structures have some resemblance to that of the normal substrate; they are analogues or caricatures of it. Normally the substrate combines with an enzyme, undergoes whatever change is brought about, and then leaves the enzyme in a state to carry out the process again. The analogue type of inhibitor upsets the process by not letting go so that the process catalyzed by that enzyme stops. If we know the chemical nature of the processes we are trying to inhibit, the search, in the light of this picture, becomes a limited search for analogues of the normal substrate. This introduces logic from the other side. As well as analysing the structure of our agents we must analyse the enzymic make-up of the process we wish to inhibit. Success depends on finding an inhibitable enzyme which is unique to the system we wish to inhibit or which is at least very much more important in this system than in any neighbouring ones.

Logically therefore the study of spermicides should wait until we know more about the biochemistry of sperm. But such a delay would be carrying logic too far. While this work is being done much would be gained if some of the firms already screening synthetic or natural substances for antibacterial activity would include the sperm of some convenient mammal in their group of test systems. Positive or negative results in such a test would not be a final answer, but they would give useful suggestions.

With many cells, even if we have a good analogue, attack is not feasible because the cell does not pick up the analogue readily. The available evidence suggests that this is less likely to cause difficulty with sperm because they are exceptionally permeable. Furthermore the exceptional composition of the fluid in which sperm are ejaculated suggests that their metabolism may be exceptional too. So far, however, this expectation has not been borne out. The field has been admirably surveyed by Mann (1949) and he concludes that much of sperm metabolism depends on systems found in most other cells; it is unlikely that these could be inhibited without causing damage to other tissues. At this stage of the discussion only the swimming of the sperm is relevant and one anomaly has been described that may be connected with it. Wajzer and Brochart (1947) claim that both boar and guinea pig sperm contain phosphoarginine. This substance plays a similar role in muscular contraction in many invertebrates to that played by phosphocreatine in mammals and it has not been found in any other part of a mammal. Its presence in sperm would have a double interest; it would be an interesting example of evolutionary "recapitulation" and it would offer a mechanism on which an *in vitro* search for inhibitors could start. Unfortunately this line of research does not seem to have been pursued and the statement has not been confirmed.

Sperm are relatively good antigens and even induce antibody formation in the same species as that from which the sperm were got. Antisera immobilize the sperm specifically (Henle, Henle and Chambers, 1938) and Parsons and Hyde (1940) have found that such antisera are effective in preventing fertilization when introduced into the vagina of the rabbit. This is encouraging, but it simply amounts to using an antibody as a specific and harmless spermicide. Some of the defects inherent in all spermicidal approaches to the problem remain. The high antigenicity of sperm has suggested to many people that it might be possible to immunize a female against sperm so that her tissues generally became toxic to them. Successes have been claimed but they have not been confirmed (cf. Parkes, 1944; Tyler, 1948) and even if it should prove possible to produce this type of immunity there is the danger that it would lead to a response similar to hay fever at any mucus surface subsequently exposed to sperm. Furthermore such immunization, if powerful enough to be effective, might well prove permanent.

The Movement of Sperm

Sperm movement deserves more study for theoretical as well as practical reasons. Sir Geoffrey Taylor (1952) has found existing hydrodynamic theory inadequate to cope with it and, as a step towards improving the theory, has had to study the movement of a model sperm driven by twisted rubber bands. This demonstration of the complexity of the problem and of the fact that theory has had to invoke simple, one might almost say crude, experimentation is very encouraging to an unashamed empiric, but it suggests that no immediately useful conclusions are likely.

The movement of sperm towards the Fallopian tube can also be obstructed by a barrier at the cervix and both primitive and more sophisticated communities have shown considerable ingenuity in constructing them. The only technique of this type that calls for consideration here depends on the fact that semen and cervical mucus do not mix readily but that actively motile sperm invade the mucus. This capacity diminishes the effect of normal spermicides because the sperm get away from them, but it opens up possibilities of rendering the mucus impenetrable. Barton and Wiesner (1951) have found *in vitro* that cetyl pyridinium chloride acts in this way and they suggest that, although it is not a spermicide, it will prevent sperm from getting into the uterus. Other surface active substances, e.g. ricinoleic acid, appear to act in the same way. This is a very interesting development in which the cervical mucus, which is constantly being renewed, is in effect being turned into an occlusive cap. The method is mentioned here, not because it has yet been fully tested, but because it illustrates a new line of biochemical thought. If

these agents are simply put in the vagina they have the defect that only mucus that has come through the cervix is exposed to them and that fresh unexposed mucus is constantly appearing. This approach would be extremely hopeful if a substance could be found that was excreted into the uterus and was then able to modify mucus in this way, but it does not seem that a substance with these properties will be found easily.

Ovulation

Sperm are produced in the testis by a complete cycle of cell division and maturation continuing throughout the period of fertility. Ova, on the other hand, appear to be formed in youth and only processes of maturation and discharge take place later (cf. Zuckerman, 1951). Maturation is under close hormonal control; this suggests that it could be inhibited. At first sight it may seem that the more elaborate process of cell multiplication which is involved in spermatogenesis would offer more opportunities for interference and it may seem that this is the process to which most attention should be paid. Cell multiplication is however probably fairly uniform throughout the body so that it is unlikely to be easily stopped in one place without being upset in other places as well. The maturation of oocytes to ova is likely to be more specific.

The literature of world travel contains many references to herbs that are eaten in primitive communities to prevent conception. As a rule the plant is left unidentified, but one, *Lithospermum ruderale*, is known to be so used by the Navajo. The extracts of the root that have been made so far are poisonous and have to be used with care, but they indubitably inhibit ovulation. The effect is apparently due to inhibition of the anterior lobe of the pituitary (Noble, Plunkett and Taylor, 1950), but circulating hormones may also be sequestrated (Skelton and Grant, 1951) and there are effects on other glands. Some of the effects can be reproduced by tannins and there is no reason to think that all are due to the same substance in these crude extracts. In their present state the extracts are not of practical use, but further work with this plant and others like it will be awaited with great interest. A general inhibition of the action of any part of the pituitary, even although it prevented ovulation or the maturation of oocytes, would create as many problems as it solved. But the discovery of specific inhibitors, either as a result of fuller knowledge of the function and action of the pituitary hormones or by following up hints from folk medicine, would present us with one of the most satisfactory methods of contraception.

The Approach and Union of the Gametes

In some species, e.g. ferns, eggs produce substances towards which sperm swim; this chemotactic action greatly increases the chance of collision and so of fertilization. Lord Rothschild (1951) has pointed out that the perception of a concentration gradient by an organism as small as a sperm involves an unusual sensitivity to small differences in concentration. If human sperm were influenced in this way it ought to be possible to attract them in the wrong direction because the amount of any substance that the ovum can secrete must be very small and it should be relatively easy to offer a counter attraction. Unfortunately, even in the sea urchin, the evidence for any such mechanism is equivocal. In mammals the gametes appear to meet in the Fallopian tube by accident and there seems to be little chance of interfering with their meeting in this way.

The actual union involves many separate processes; these are to some extent understood and hold out good hopes of inhibition. Mammalian ova have probably never been fertilized *in vitro* (Austin, 1951; Smith, 1951), but Moricard (1950) has fertilized them in pieces of isolated Fallopian tube. The nature of the contribution made by the tube is not understood, but it would repay study for it might be specific and inhibitable. Although the whole process cannot be studied *in vitro* useful information has been gained about different aspects of it.

The first barrier that the sperm has to pass is the gelatinous mass of cumulus or follicle cells surrounding the ovum. This mass can

readily be dispersed by the enzyme hyaluronidase which is found in the testis and in or on sperm. The obvious interpretation is that the sperm gets through because of the presence of hyaluronidase (McClean and Rowlands, 1942) and the corollary of this, since the enzyme is found in few other places in the mammalian body if indeed in any, is that if the enzyme were inhibited penetration would be impaired or prevented. Hadidian and Pirie (1948) found that nitrated hyaluronic acid inhibited the enzyme and Pincus, Pirie and Chang (1948) found that it inhibited the dispersal of cumulus cells *in vitro* and acted as a contraceptive when put into rabbits' vaginas before mating. Martin and Beiler (1952) have used the same idea to better effect by giving phosphorylated hesperidin, which is also an inhibitor of hyaluronidase, by injection and by mouth. In rats it reduced fertility to one-fifth without being toxic or affecting œstrus. These results are encouraging because a selective enzyme inhibitor could be used at higher concentrations than the types of substance used hitherto as spermicides. If something even better than phospho-hesperidin can be found which works by a route other than the vagina the prospects are hopeful. Vaginal hyaluronidase inhibitors do not immobilize sperm, so that they will be ineffective unless they can remove or permanently inhibit the enzyme during the period of contact in the vagina; this capacity has not been demonstrated. It is claimed that the importance of hyaluronidase has been exaggerated because rabbit eggs have been found that are fertilized although still surrounded by cumulus cells; but for fertilization it is only necessary for the sperm to make a tunnel large enough for it to get through and there is no reason why such a tunnel should be visible. A powerful and harmless antihyaluronidase would not necessarily be a practical contraceptive, but the possibility seems good.

Having passed the layer of cumulus cells the sperm meets first the zona pellucida and then the vitellus. Austin (1951) finds that rat sperm make a slit in the zona and suggests that this is due to the action of a mucolytic enzyme whose action is favoured by an acid and reducing environment. There is no detailed information about the nature of this action and therefore no reason to think that it will be more easily inhibited than hyaluronidase. The same difficulties apply; the inhibitor is put in at one place in the hope that it will act at another. Nothing is known about the biochemistry of the penetration of the vitellus. Two sperm rarely get into one ovum; the surface becomes impenetrable soon after one sperm has passed through it. Much is known about this phenomenon but its mechanism is still obscure and it deserves still further study. What a sperm can do a biochemist should be able to do also.

The Implantation of the Zygote

The fertilized ovum moves down into the uterus and erodes an attachment site for itself. By the time attachment is complete and a placenta has begun to form the problem has passed beyond the scope of this paper, but many biochemical processes are involved during the period of attachment. It is now generally agreed that deficiency in either progesterone or vitamin E impairs attachment and work is proceeding on the possibilities of simulating such a deficiency with analogues to either substance. This method of approach has the great advantage that the agent would probably be given by some other route than the vagina and its effects would last for several weeks at least. Unfortunately no results have been published as yet that suggest that the problem has been solved, but there have been some statements in the popular Press suggesting that results are encouraging. A method that may have a somewhat similar rationale is the Grafenberg ring which was used extensively twenty years ago but was then nearly universally condemned. A loop of silver wire in the uterus irritates the endometrium sufficiently to prevent implantation as a rule. But implantation sometimes takes place in spite of it and the ring may come out or get corroded. For these reasons the popularity of the method has declined, but there may still be the germ of an idea here. If the action is predominantly mechanical it

may be that another metal, such as tantalum or stainless steel, would be more suitable than silver. If on the other hand the action is chemical and the slow corrosion of the ring is an essential part of the process, research is called for to see if the results would not be better with slowly dispersing pellets than with the rings used now.

All the subjects for research that have been discussed so far have certainty as their object; they have been treated from the standpoint of the prevention of conception although, as has been pointed out, the same knowledge is likely to be of use in certain cases of involuntary sterility. The survey of present knowledge and future prospects has been unavoidably brief and a table may make the sequence of events and their relative vulnerability clearer. It is hardly to be expected that those familiar with the subject will agree with all the judgments made on such imponderables as the extent of knowledge in different fields and the probabilities of success in research. All that can be hoped for is that absurdities have been avoided. For the sake of simplicity the table has been limited to biochemical aspects of the problem.

SYNOPSIS OF THE SUBJECTS CONSIDERED AND OF THEIR USEFULNESS IN CONTRACEPTION

Subject	Present information	Prospects for inhibition	Probability of specificity	Probability of satisfactoriness
Spermatogenesis	fair	good	little	little
Sperm maturation	little	—	—	—
Semen composition and texture	good	good	good	some
Sperm motility	fair	good	good	some
Movement through cervix	some	good	good	fair
Oogenesis	little	poor	poor	poor
Ovum maturation and discharge	fair	good	fair	fair
Ovum movement	little	—	—	—
Meeting of the gametes	little	—	—	—
Union of the gametes				
Traversing of 1. cumulus	good	good	good	fair
2. zona pellucida	little	—	—	—
3. vitellus	none	—	—	—
Movement of zygote	little	—	—	—
Implantation of zygote	good	good	good	good

Social Influences on Fertility

The problem is not however limited to techniques that have certainty as their object. Much could be done to change a population trend if the general fecundity were altered so that the same amount of sexual activity led to a different number of pregnancies. This could be the result of a relatively trivial change. Thus it has been suggested that the decline in fertility which generally accompanies a rise in the standard of living is due to the more widespread use of soap, for soap is a potent spermicide. Furthermore, changes in hygienic customs affect the bacterial flora of the vagina and cervix and this probably affects fecundity. The suggestion has indeed been made that floral changes could be made deliberately which would promote or discourage fertility. The decline has also been attributed to the increase in protein intake that generally accompanies a rise in the standard of living, but most of the experiments carried out with animals do not substantiate this suggestion and so many things alter when the standard of living alters that it is unreasonable to pick on one of them without further evidence. The effects of variation in the intake of protein, vitamins and other nutrients were analysed at a symposium on " Nutrition and Fertility " that the Nutrition Society held in 1949; the record bristles with suggestions for further work, but nothing immediately applicable emerged.

The behaviour pattern of a community affects its fertility in many other ways. Thus the hormonal interrelations of lactation and ovulation diminish the likelihood of another pregnancy in the period while a child is being suckled. This is important in many primitive communities where weaning, on our contemporary standards, is delayed. But Shakespeare accepted without surprise the weaning of Juliet at three. The experience seems to have done her no harm; she was responsive enough at fourteen. In an industrialized community, however, delayed weaning would have disadvantages. The precise effect of each social change on fecundity has not been, and perhaps cannot be, ascertained and it is unprofitable to pursue the matter further for we are in a realm in which fad takes precedence over fact. In any event, in spite of Hecate's assertion that " —security is mortal's chiefest enemy " this is a field in which most people value security above a mere alteration in the odds however important that may be demographically.

Factors Discouraging Research

It is obvious that there is no shortage of problems in a study of the gametes, their union and the development of the zygote. From the appearance recently of several excellent reviews (Tyler 1948, Mann 1949, *Biochemical Soc. Symp.* 1951, Rothschild 1952) it is also clear that there is a growing awareness of the intrinsic interest of the subject. The need for intensive work on the application of this knowledge to contraception is less widely recognized or accepted. On the one hand one gets told " Work is being done on that; there is so-and-so and so-and-so." This misconceives the amount of work that will probably be necessary. It is only because more than a hundred able scientists have studied pepsin during the last hundred years that we can now make adequate technological use of it. If as much work had been done on hyaluronidase we would be using it for something, though possibly not contraception. To take a more recent example: antibiotics do not yet give complete satisfaction in spite of the 10 to 100 million able man-hours that have already been expended on their development and improvement.

On the other hand one is told that existing methods are not so bad. " Not so bad as what? " is the obvious reply. Clearly they are better than nothing and every form of help and encouragement should be given to those who spread knowledge of them. But even among people in a civilized environment they fall short of perfection and are largely impractical among more primitive peoples. It is no use arguing that they would be adequate if people were more sensible. The fact that people are sometimes silly must be recognized and it is as unreasonable to devise a contraceptive method that disregards this as it would be to devise one that depended on sperm having properties different from those they are known to have. No method can be looked on as fully satisfactory unless it has such a margin of safety as to remain effective even when used with some lack of skill. Furthermore a satisfactory method should require only infrequent attention, otherwise a revulsion against the whole business (cf. Mitchison, 1930) may be built up. This would certainly solve one problem, but only at the cost of introducing another. The facts of psychology, inconvenient as they may be, are as real as the facts of biochemistry.

The Royal Commission on Population, reporting in 1949, fully recognized the defects of present methods. The Commission's words are worth quoting (para. 427): "Control by men and women over the numbers of their children is one of the first conditions of their own and the community's welfare and in our view mechanical and chemical methods of contraception have to be accepted as part of the modern means, however imperfect, by which it can be exercised." The Commission makes no proposals about how these recognized imperfections could be remedied; its acceptance of them has the sublimity of Margaret Fuller's remark " I accept the Universe." To this Thomas Carlyle responded " By God! she'd better." Fortunately there is no similar compulsion in this instance and we

may go on to consider how and by whom the necessary research could be done.

Potential Supporters of Research

Pressure of population and shortage of food are such well-known stimulants to aggression that the international bodies such as the World Health Organization and FAO have an obvious interest. At present they seem to be more concerned with medical services, which exacerbate the problem, and with arranging for food shipments and improvements in agriculture, which are palliatives. There is as yet no sign that the world organizations have recognized that there is a population limit somewhere and that we are not equipped with the information to deal with the problems that will arise when we seem to be getting close to it. When it is possible to plan at least the upper limit of a country's population there will be one simple criterion of aggressive intent; the ratio of population to food supply. During the last half-century there have been several examples of deliberate attempts by governments to create a population problem, even in hungry countries, by encouraging fecundity. The idea is not new; it was apparent to Shakespeare when he wrote

> "To't luxury, pell mell! for I lack soldiers."

But Lear was mad when he said that; more recent users of the same argument are sometimes not so judged. Hitherto an expanding population has found room by filling an empty area or by shoving the earlier occupants out of a filled one. We from Britain have done both exuberantly and we are open to the charge of hypocrisy if we now say that other people should not follow our bad example but should try to live within their present domain and on its produce. There is no fairness in our plea; we had our turn of expansion, why should not others have theirs? There is no fairness but there is some practical sense. It is practical, if immoral, to replace the occupants of a filled land when there is a great disparity in the technical attainments of the two sides. There are few areas in which this disparity still exists so that what looks like hypocrisy may in fact be the beginnings of wisdom.

The nations fall into three fairly distinct categories; some have already an obvious population problem but lack the research organization to do anything about it, at least along the lines suggested in this paper. Others, notably Britain and similar industrialized countries, feed precariously with their present populations. A few countries still seem to have ample food. We in the middle group have a special responsibility, we not only need the knowledge ourselves but we have a duty to help the others. In the past we have shown great missionary zeal in spreading education round the world and in undertaking a wide range of activities for other peoples less able to cope with them; it may be that we should undertake research for the world also.

The best reason why we should undertake research on contraception is that the results would probably be welcomed by most of our own population. There are other reasons and one important one is that this research should diminish the number of illegal abortions. There are no accurate figures, but the rate may safely be put at 50,000—100,000 annually in this country and some authorities give an even higher figure. Even under proper conditions abortion is not to be undertaken lightly; under the inadequate conditions created by illegality it is a major health hazard and a cause of subsequent ill-health. There are many diseases which affect a much smaller proportion of the population while having well-financed, and deservedly well-financed, research organizations examining their prevention and cure. The fact that abortion is illegal and is entered upon voluntarily does not affect the medical issue. Medicine is concerned with the protection of people from the consequences of their deliberate even if foolish actions as much as with their protection from other causes of ill-health. We are concerned simply with the question: How many abortions are due to the failure of contraception? Only a guess can be made, but it is very unlikely that the number is less than half of the total. We do not therefore have

to go to distant or primitive peoples to find a reason for wanting more research on contraception—it is on our doorsteps and in the back streets. And it is there on a scale that seems amply large enough to justify official recognition and the establishment of a research unit.

There are many other types of organization that should support, or at least not obstruct, this research and prominent among them are the religious and ethical communities. Even if we accept the view of some religious groups that erotic satisfaction to an extent greater than that needed to maintain the population is to be deplored, it still seems unethical to use a child as the sanction for promoting this viewpoint. Similarly, fear of pregnancy seems to be a poor method of enforcing a moral code on those who are not married. If an ethical belief is worth having it is worth having for its own sake and lapses from it should carry a spiritual rather than a domestic penalty; there can be no proof that the belief is genuine for as long as a lapse may be followed by physical consequences. Much emotional distress is caused by unattained or unwanted pregnancies and it would seem to be as much the business of the Churches now to help in avoiding the consequent personal and national troubles as it was the business of the Church in the Middle Ages to organize the hospitals.

Finally there are bodies such as the *Eugenics Society*. Clearly there can be no eugenics unless births are in some way controlled. At present contraception works dysgenically if at all. In the popular phrase we breed from the "reckless and the feckless" and the descendants of the careless and the inexpert are a growing community. If all births were deliberate there might well be a sharp decline in the population, but it would be a controlled decline for we should always be breeding from the most philoprogenitive section of the community. If philoprogenitiveness is inherited there will therefore be no need to fear national extinction, for as soon as it appears that a larger population is feasible or desirable expansion is likely to be immediate (cf. Blacker, 1950). As time goes on the awareness of social responsibility becomes more widespread in the community and it becomes easier to persuade those who carry undesirable traits that it would be a mistake for them to have children. In general the more they want children the easier it is to persuade them of this because the positive wish to have children is often part of a socially responsible attitude. For the rest the availability of fully adequate contraception should solve the problem. The motive behind most copulation is sex and not procreation. Housman's dictum

> The night my father got me
> His mind was not on me;

is a fairly adequate summary of the matter. Until a sustained attempt to get voluntary eugenics has been made, and has failed in spite of the provision of an irreproachable contraceptive technique, there is no case for advocating further legal restrictions. The scientist is not entitled to advocate further restrictions on childbearing, with all the social and emotional complications they involve, until the research that he has done is beyond criticism.

In pursuing the question of how to get the necessary enormous amount of work done on the gametes we come in the end to the research worker. There is no need to enlarge on the intrinsic interest of the problem; it is obvious, and has already been commented on briefly (Pirie, 1952). This alone, were it not for a certain prudery and the relative inaccessibility of the research material, should have got much of the necessary work done long ago. Material is now becoming more accessible and, as has been pointed out, there is an increasing recognition of the theme. Scientists respond to much the same set of stimuli as other people; if ordered about they are obstructive, if flattered a little and offered opportunities they tend to co-operate. If the public moved angrily, even if democratically, and said, as in my view it would be thoroughly justified in saying, "What do you people think you are doing occupying all these buildings and spending all these millions every year while we still have to put up with the common cold and messy, inadequate and archaic methods

of contraception ! " we scientists would talk smoothly of the difficulties and dangers and the necessity for hastening slowly. We might convince our critics, but would we convince each other? More important, would we convince ourselves?

There is no agreement about the imminence of world overpopulation. In some quarters there is near panic, whereas the contributors to *Four Thousand Million Mouths*, by emphasising the unexploited possibilities of getting more food, suggested that we have a little time at our disposal. At present erotics and fecundity are entangled. The thesis of this paper is that with adequate research they could be dissociated. Once a community had an emotionally and æsthetically satisfactory contraceptive technique the birth-rate would reflect the demand for children and nothing else. Without any coercion a birth-rate compatible with space and food supplies would then be achieved. This is of course a pure assumption, but it seems plausible and there is no acceptable alternative. It is clear that many social, moral and political consequences would follow the establishment of this dissociation. With these we are not here concerned; equally serious though different consequences will follow the failure to establish it. But no control can be established until we have much more knowledge, and research on the necessary scale is not yet being done.

Summary

Present methods of contraception are extremely useful and should be made more widely known, but they fall short of perfection both on the score of reliability and æsthetics. They have been produced mainly by *ad hoc* research and the argument is developed that better results would follow a more elaborate and thorough investigation of the biochemistry and physiology of sperm and ovum and of the whole process of their union, and of the development of the zygote. This information would also help in preventing some involuntary sterility. The existing body of knowledge is surveyed cursorily and suggestions are made about the more promising lines.

A very great deal of work will probably be needed before fully satisfactory methods of contraception are developed and a few suggestions are made about the organizations or groups that might finance it and about the arguments that could be used to persuade them to do so.

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